

Excerpts from the Opinion on *in vitro* methods to assess skin corrosivity in the safety evaluation of cosmetic ingredients or mixtures of ingredients adopted by the plenary session of the Scientific Committee for Cosmetic Products, and Non-food Products intended for Consumers (SCCNFP) of 25 November 1998 as obtained from the Internet at

http://europa.eu.int/comm/food/fs/sc/sccp/out47_en.html

Outcome of discussions

Terms of Reference

Two *in vitro* methods developed to assess skin corrosivity of chemicals, the "Rat skin Transcutaneous Electrical Resistance (TER) test" and the "EPISKIN test" have been validated by ESAC (ECVAM Scientific Advisory Committee). The Scientific Committee on Cosmetic Products and Non-Food Products (SCCNFP) has been requested by DG III to advise the Commission on the applicability of the methods to the safety assessment of chemicals used as cosmetic ingredients.

Background

The European Centre for the Validation of Alternative Methods (ECVAM) has conducted in 1996-1997 a validation study of *in vitro* tests developed to assess skin corrosivity of chemicals. This study was a follow-up to a pre-validation study of tests developed for replacing the *in vivo* Draize skin corrosivity test in rabbits. The main objectives of the validation study, as defined by the sponsors and the management team before the study began, were :

- (a) to identify tests capable of discriminating corrosives (C) from non corrosive (NC) for selected groups of chemicals (e.g. organic acids, phenols) and/or all chemicals (single chemical entities only);
- (b) to determine whether the tests could identify correctly known R35 (UN packing group I) and R34 (UN packing groups II & III) chemicals.

Organisation of the study

The study was coordinated from ECVAM. A Management Team (MT) was constituted by four representatives of lead laboratories, each of them being responsible for one of the four tests being evaluated. The tests selected for inclusion in the validation study were the rat transcutaneous electrical resistance (TER) test, Corrositex, the Skin² ZK1350 corrosivity test, and Episkin. Each test was conducted in three different laboratories, according to principles, criteria and procedures previously defined by ECVAM. Prediction models for each of the four tests were defined in the test protocols.

Coordination /MT /Laboratories

Sixty chemicals were selected by an independent Chemicals Selection Sub-Committee, and distributed coded to the participating laboratories. These included organic acids (6C/5NC), organic bases (7C/3NC), neutral organics (9NC), phenols (2C/3NC), inorganic acids (6C/1NC), inorganic bases (2C/2NC), inorganic salts (1C/2NC), electrophiles (3C/5NC), and soaps/surfactants (3NC). The selection is fully described in a publication (Ref. 1); the main criterion for including chemicals in the test set was that the corrosivity classifications were based on unequivocal animal data.

The results obtained were analysed by statistician experts. The classifications of the corrosivity potential of the test chemicals, as derived from the *in vitro* data obtained in the three laboratories conducting the test, were compared to the *in vivo* classifications independently assigned to the chemicals before the blind trial, to yield sensitivity, specificity, predictivity and accuracy of the test.

Main results

The full details of the validation study have been published (Ref. 2). Two tests, with a good reproductibility within and between test laboratories, proved applicable to the testing of a diverse group of chemicals: the TER test and Episkin.

In the TER test, test materials are applied for 2 to 24 hours to the epidermal surface of skin discs taken from the pelts of humanely killed young rats, and corrosive chemicals are identified by their ability to produce a loss of normal stratum corneum integrity, which is measured as a reduction of the inherent transcutaneous electrical resistance (below a predetermined threshold level).

Episkin is a tri-dimensional human skin model with a reconstructed epidermis and a functional stratum corneum. When utilised in corrosivity testing, application of test chemicals to the surface of the skin for 3, 60 and 240 min, is followed by an assessment of cell viability.

Sensitivity, specificity, predictivity and accuracy in distinguishing corrosive from non corrosive chemicals were very high for both tests: 88, 72, 72, 79 and 83, 80, 77, 81% respectively for the TER test and Episkin. In addition, Episkin was also able to distinguish between known R35 (UN packing group I) and R34 (UN packing groups II & III) chemicals.

Opinion of the SCCNFP

ECVAM Scientific Advisory Committee (ESAC), which had been fully informed of the progression of the validation procedure, reviewed the final results and unanimously endorsed a statement that the rat skin TER test is scientifically validated for use as a replacement for the animal test for distinguishing between corrosive and noncorrosive chemicals, and that Episkin is scientifically validated as a replacement for the animal test, and that these tests are ready for regulatory acceptance.

Sixty chemicals were used for the validation of these two methodologies; twenty of them are used as cosmetic ingredients, according to the "European inventory and common nomenclature of ingredients employed in cosmetic products" (Ref. 3).

SCCNFP reviewed publications from the validation study and ESAC statements, and propose that these two methods could be applied to the safety assessment of chemicals used as cosmetic ingredients. A cosmetic ingredient or mixture of ingredients can be corrosive per se. When corrosivity cannot be excluded, testing for irritancy on animals or humans should be preceded by a corrosivity test using one of these two validated *in vitro* methodologies.

References

- 1- Barratt M.D. & al. Toxicology in Vitro (1998) 12, 471-482
- 2- Barratt M.D. & al. Toxicology in Vitro (1998) 12, 483-524
- 3- Commission Decision 96/335 EC of 8 May 1996 establishing an inventory and a common nomenclature of ingredients employed in cosmetic products J.O. L 132 of 1 June 1996

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